Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

Claims 5-8, 11-13, 16, 19, 27, 29, 34, 41, 42, 45-47, 50, 53, 63, and 70 have been canceled without prejudice; claims 1, 9, 14, 15, 17, 18, 20, 21, 43, 44, 48, 49, 51, 52, 54, and 55 have been amended; and new claims 74-78 have been added. Descriptive support for the subject matter of new claims 74-77 is respectively provided, e.g., in claims 22, 23, 30, and 58 as filed. Descriptive support for the subject matter of new claim 78 appears in the paragraph bridging pages 20-21. Claims 1-4, 9, 10, 14, 15, 17, 18, 20-26, 28, 30-33, 35-40, 43, 44, 48, 49, 51, 52, 54-62, 64-69, and 71-78 are pending.

The objection to claims 35, 38, 40, 64, 67, and 69 under 37 CFR 1.75(c) for failing to further limit the subject matter of a previous claim is respectfully traversed. Each of the objected-to claims contains a Markush group reciting different genera of oomycetes. Hence, the recited Markush group is distinct of and necessarily limits the claim language "oomycete" that appears in the independent claim. For this reason, the objection is improper and should be withdrawn.

The objections to claims 14-15, 17-18, 20-21, 48-49, 51-52, and 54-55 are overcome by the above amendments.

The rejection of claims 1-73 under 35 U.S.C. § 112 (first paragraph) for lack of enablement is rendered moot with respect to the canceled claims, and is otherwise traversed with respect to claim 1 (and claims dependent thereon) in view of the above amendments and the following remarks.

The PTO has asserted at page 6 of the outstanding office action that Bauer et al., *Acta Hort.* 489:301-304 (1999) ("Bauer 1999") showed the necessity of a secretion signal. The PTO's position is misplaced. Bauer 1999 at page 302 reports the following results:

> All control plants (wild type and transgenics without *hrpN*) displayed sporulating lesions by 7-10 days after inoculation, the peak of the disease cycle. In contrast, transgenic *Arabidopsis* containing *hrpN* under the control of P_{Gst1} were completely free of signs of disease 10 days after inoculation. *Plants containing the* hrpN *construct lacking a signal sequence showed signs of infection 16 days after inoculation, but the number of sporangia per leaf and the symptoms such as growth reduction and lesion formation was much less than in control plants* (emphasis added). Most plants

> containing the *hrpN* construct with the signal sequence remained free of any signs of the pathogen. Only a small portion, ca. 10%, showed signs of disease any time after inoculation.

Thus, Bauer 1999 actually shows that the secretion signal afforded the best results, but that absent the secretion signal, the P_{Gst1}::*hrpN* construct was able to reduce the severity of and the onset of infection. The secretion signal, therefore, is not necessary for operability. For this reason, and in view of the above amendments, the rejection of claims 1-72 for lack of enablement is improper and should be withdrawn.

Applicants respectfully traverse the rejection of claim 73. For the reasons noted below in response to the rejection of claim 73 as lacking written descriptive support, applicants submit that one of skill in the art is fully able to identify other hypersensitive response elicitor-encoding nucleic acid from bacterial plant pathogens (as applicants and others have done), and then utilize those nucleic acids in the preparation of chimeric genes and transgenic plants of the present invention, for example, in the manner described in Examples 1-3 of the present application for preparation of *hrpN* constructs. For these reasons, the rejection for lack of enablement is improper and should be withdrawn.

The rejection of claims 1-73 under 35 U.S.C. § 112 (first paragraph) as lacking written descriptive support is rendered moot with respect to the canceled claims, and is otherwise traversed with respect to claim 1 (and claims dependent thereon) in view of the above amendments.

Applicants respectfully traverse the rejection of claim 73. The PTO has taken the position at pages 9-12 of the outstanding office action that the four exemplary nucleic acids (SEQ ID NO: 2 encoding HrpN of *Erwinia chrysanthemi*, SEQ ID NO: 4 encoding HrpN of *Erwinia amylovora*, SEQ ID NO: 6 encoding HrpZ of *Pseudomonas syringae*, and SEQ ID NO: 8 encoding PopA1 of *Pseudomonas solanacearum*) are not representative of the claimed genus. The basis for the PTO's position is that a number of pathogen species—in the sense of biological classification—exist, and hypersensitive response elicitors from only several of the many pathogen species have been described in the specification. Applicants submit that this basis for asserting lack of written descriptive support is insufficient.

The Federal Circuit has clearly espoused that *per se* conclusions of written description violations cannot be founded upon the basis of genus size alone. *See Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 1326-27, 63 USPQ2d 1609, 1614-15 (Fed. Cir. 2002) (refusing to adopt position that three species as a matter of law cannot satisfy written description requirement for significantly larger genus). Thus, the PTO's conclusion cannot be based on genus size alone. But that is precisely what the PTO has done at pages 9-

12 of the outstanding office action. The PTO lists numerous organisms, suggests that the majority of these organisms would produce at least one hypersensitive response elicitor, and then concludes that neither the claimed genus nor the subgenera from any bacteria are adequately described. Because the PTO's position is unsupported by law and unsupported by any facts other than genus size, applicants submit that the PTO's position cannot be sustained.

With respect to the PTO's citation of several hypersensitive response elicitors identified after the priority filing date of the present application (e.g., HrpW of *Erwinia amylovora* and *Pseudomonas syringae*), it should be noted that the specification teaches those of skill in the art that these elicitors, too, can be used to practice the invention even though their nucleotide and amino acid sequences are not recited specifically in the specification. It should be noted that the "Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112 ¶ 1, 'Written Description' Requirement," make explicitly clear that the description of a representative number of species does *not* require the description to be of such a nature that it would provide support for each species that the genus embraces. 66 Fed. Reg. 1099, 1106 (2001). Hence, the absence of sequences for the later-identified HrpW elicitors, or any other Hrp elicitors, is irrelevant to the issue of whether the present specification provides adequate written descriptive support for their use in accordance with the present invention.

Moreover, the conclusion by the PTO is contrary to evidence previously submitted by applicants. As demonstrated by the Declaration of Zhong-Min Wei Under 37 C.F.R. § 1.132 ("Wei Declaration")(submitted with response dated July 30, 2003), one of ordinary skill in the art would have understood that applicants were in possession of the presently claimed invention at the time the present application was filed. This is so, because the four exemplary species were recognized at the time of filing as belonging to an art-recognized class of hypersensitive response eliciting proteins produced by bacterial plant pathogens.

One reason why the disclosed species are representative of the claimed genus is because the species were recognized as structurally and functionally conserved. For example, it was known that hypersensitive response elicitors within a given genus—again, in the sense of biological classification—are often homologous to elicitors from different pathogenic species and strains of the same genus. *See* Wei Declaration ¶ 6. This has been demonstrated among HrpN homologs from *Erwinia*, where the *Erwinia amylovora hrpN* gene has been used to clone other *hrpN* homologs from different *Erwinia* species (*see* Wei Declaration ¶¶ 7-9); and HrpZ homologs from *Pseudomonas*, where the *Pseudomonas*

syringae hrpZ gene has been used to clone other *hrpZ* homologs from different *Pseudomonas syringae* pathovars (*see* Wei Declaration ¶ 10). Thus, one of ordinary skill in the art would expect structural conservation of hypersensitive response elicitors, at least among the pathogens classified as belonging to the same genus (again, in the sense of biological classification).

Another reason why the disclosed species are representative of the claimed genus is because the encoding genes are similarly regulated, expressed, and secreted by their source organisms. For instance, the genes encoding hypersensitive response elicitors are positioned within the *hrp* gene cluster or proximate to the *hrp* gene cluster in *hrp* regulons. *See* Wei Declaration ¶ 11. Substantially all hypersensitive response elicitors identified have been shown to be secreted through the type III (or *hrp*-dependent) secretion pathway, which is a highly conserved and unique mechanism for the delivery of pathogenicity related molecules in gram-negative bacteria. *See* Wei Declaration ¶ 13. Finally, expression of the genes encoding the *hrp* gene cluster is induced under conditions that mimic the plant apoplast, such as low concentrations of carbon and nitrogen, low temperature, and low pH. *See* Wei Declaration ¶ 14. Thus, because the encoding genes are similarly regulated, expressed, and secreted by their source organisms, one of ordinary skill in the art would expect other hypersensitive response elicitor genes to behave similarly.

Another reason why the disclosed species are representative of the claimed genus is because the disclosed species are characterized by a number of common biochemical characteristics which were known to those of skill in the art prior to the filing date of the present application. These include being glycine rich, heat stable, hydrophilic, lacking of an N-terminal signal sequence, and susceptible to proteolysis. *See* Wei Declaration ¶ 15.

A final reason why the disclosed species are representative of the claimed genus is because these species share the ability to induce specific plant responses. The induction of plant disease resistance, plant growth enhancement, and plant stress resistance are three plant responses that result from treatment of plants or plant seeds with a hypersensitive response elicitor from a bacterial plant pathogen. *See* Wei Declaration ¶ 17. With respect to disease resistance, topical application of HrpN from *Erwinia amylovora* resulted in disease resistance to plants for a broad range of plant pathogens (*see* Wei Declaration ¶ 18), topical application of HrpZ from *Pseudomonas syringae* resulted in disease resistance to plants for a diverse range of plant pathogens (*see* Wei Declaration ¶ 19), and topical application of HreX from *Xanthomonas campestris* resulted in disease resistance to plants for a range of plant pathogens (*see* Wei Declaration ¶¶ 21-23). This ability to induce disease resistance via topical application also has been borne-out via transgenic

expression as described in the present application and reported in Bauer 1999 (cited above). Because disease resistance has been demonstrated generally for topical application of HrpN of *Erwinia amylovora*, HrpZ of *Pseudomonas syringae*, and HreX of *Xanthomonas campestris*, and oomycete resistance has been demonstrated for transgenic expression of *hrpN* of *Erwinia amylovora* in accordance with the present invention, one of ordinary skill in the art would expect other members of this art-recognized class to likewise induce oomycete resistance in plants following transgenic expression thereof in accordance with the present invention (*see* Wei Declaration ¶ 4).

Thus, applicants have presented a body of evidence demonstrating that the four species belong to an art-recognized class of proteins from bacterial plant pathogens; that structural conservation exists among homologs of the different hypersensitive response elicitor proteins; that hypersensitive response elicitor genes are similarly regulated, expressed, and secreted by type III secretion systems of their source organisms; that the hypersensitive response elicitor proteins are characterized by a number of common biochemical characteristics which were known to those of skill in the art prior to the filing date of the present application; and that the hypersensitive response elicitor proteins of this art-recognized class are functionally similar in their ability to induce similar plant responses, including induced oomycete resistance in accordance with the present invention. The PTO, on the other hand, has merely suggested that the genus is large and may contain many species—though the PTO did not demonstrate that the genus contains structurally and functionally unrelated species.

For all these reasons, the rejection of claim 73 as lacking written descriptive support is improper and should be withdrawn.

The rejection of claims 1-73 under 35 U.S.C. § 112 (second paragraph) for indefiniteness is overcome with respect to claim 1 and claims dependent thereon in view of the above amendments.

Applicants respectfully traverse the rejection of claim 73. In particular, applicants submit that the claim language "glycine rich" and "substantially no cysteine" are not indefinite. Relative language is not *per se* indefinite. In particular, the definiteness of claim language must be considered, instead, in light of the specification, the prior art, and the claim interpretation that would be given by one of ordinary skill in the art. *See In re Marosi*, 710 F.2d 799, 218 USPQ 289 (Fed. Cir. 1983); *Rosemount, Inc. v. Beckman Instruments Inc.*, 727 F.2d 1540, 221 USPQ 1 (Fed. Cir. 1984); *W.L. Gore & Assoc., Inc. v, Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983). For example, in *In re Marosi*, the Federal Circuit found that the claim language "essentially free of alkali metal" was not indefinite

(even though—as argued by the PTO—the language could mean anywhere from between 4 ppm to 3819 ppm) and did not require the inventor to recite a particular number to define the meaning of this term. *Id.* at 802-803, 218 USPQ 292-293. In this case, "glycine rich" and "substantially no cysteine" are terms that one of ordinary skill in the art would fully understand.

In both the years preceding the filing date of the present application and thereafter, persons of skill in the art routinely used the term "glycine rich" to describe this same class of bacterial hypersensitive response elicitor proteins. *See*, *e.g.*, Bonas, "Bacterial Home Goal by Harpins," *Trends Microbiol.* 2: 1-2 (1994) ("Bones I") (copy attached as Exhibit 1 to response filed April 22, 2002) at 1, center column; Bonas, "*hrp* Genes of Phytopathogneic Bacteria," *Current Topics in Microbiology and Immunology* 192: 79-98 (1994) ("Bonas II") (copy attached as Exhibit 2 to response filed April 22, 2002) at 89-90; and Preston et. al., "The HrpZ Proteins of *Pseudomonas syringae* pvs. *syringae, glycinea,* and *tomato* are Encoded by an Operon Containing *Yersinia ysc* Homologs and Elicit the Hypersensitive Response in Tomato but not Soybean," *MPMI* 8(5): 717-32 (1995) ("Preston") (copy attached as Exhibit 3 to response filed April 22, 2002) at 718, left column; Büttner et al., "Getting Across — Bacterial Type III Effector Proteins on Their Way to the Plant Cell," *EMBO Journal* 21(20):5313-5322 (2002) ("Büttner") (copy attached as Exhibit 1 to response filed May 5, 2004) at 5318, left column; and Alfano et al., "Minireview: The Type III (Hrp) Secretion Pathway of Plant Pathogenic Bacteria: Trafficking Harpins, Avr Proteins, and Death," *J. Bacteriol.* 179(18):5655-5662 (1997) ("Alfano") (copy attached as Exhibit 2 to response filed May 5, 2004) at 5657, right column. Thus, while "glycine rich" does not define a numerical value, it is clear that persons of skill in the art fully appreciate this term of art.

Most definitions of this class of bacterial hypersensitive response elicitor proteins utilize the language "lacks cysteine" rather than the claim language "substantially no cysteine." *See*, *e.g.*, Bonas I, Bonas II, Preston, Büttner, Alfano. The claim language certainly encompasses the possibility that a cysteine residue may be present, as is the case with the subsequently identified elicitor HreX from *Xanthomonas campestris*, which contains a single cysteine residue. With only a single cysteine residue, even HreX would be unable to form disulfide (cys-cys) bonds. Persons of skill in the art would fully understand, therefore, that "substantially no cysteine" would encompass those elicitor proteins that contain no more than one cysteine residue.

For these reasons, applicants submit that the presently recited claim language is not indefinite and the rejection of claim 73 should therefore be withdrawn.

The rejection of claim 1, 7-27, 30, 35-61, and 64-72 under 35 U.S.C. § 103(a) for obviousness over U.S. Patent No. 5,850,015 to Bauer et al. ("Bauer '015") in view of each of Doerner et al., *Bio/Technol.* 8:845-848 (1990) ("Doerner") and Kawamata et al., *Plant Cell Phsysiol.* 38:792-803 (1997) ("Kawamata") is respectfully traversed in view of the above amendments. The combination of references fails to teach or suggest the presently claimed chimeric gene, which includes "the promoter comprising nt 295-567 of SEQ ID NO: 9." For this reason, the rejection should be withdrawn.

The rejection of claims 2-4, 28, 31-33, and under 35 U.S.C. § 103(a) for obviousness over Bauer '015 in view of each of Doerner and Kawamata (as cited above), and further in view of Gopalan et al., *Plant Cell* 8:1095-1105 (1996) is respectively traversed in view of the above amendments. The combination of references fails to teach or suggest the presently claimed chimeric gene, which includes "the promoter comprising nt 295-567 of SEQ ID NO: 9." For this reason, the rejection should be withdrawn.

The rejection of claims 1-2, 7-28, 30-31, 35-44, 56-62, and 64-72 under 35 U.S.C. § 103(a) for obviousness over U.S. Patent No. 5,981,843 to Chappell et al. in view of U.S. Patent No. 5,977,060 to Zitter et al. is respectfully traversed. The combination of references fails to teach or suggest the presently claimed chimeric gene, which includes "the promoter comprising nt 295-567 of SEQ ID NO: 9." For this reason, the rejection should be withdrawn.

In view of all the foregoing, it is submitted that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

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Edwin V. Merkel
Registration No. 40,087

NIXON PEABODY LLP
Clinton Square, P.O. Box 31051
Rochester, New York 14603
Telephone: (585) 263-1128
Facsimile: (585) 263-1600

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